REMARKS

Favorable reconsideration is respectfully requested in view of the foregoing amendments and the following remarks.

I. CLAIM STATUS AND AMENDMENTS

Claims 1-3 were pending in this application when last examined and stand rejected.

Claims 1-3 were objected to.

Claims 1-3 have been amended to appropriately recite the definitions for the abbreviated terminology. Support for the definition of "ERRL1" as "an estrogen related receptor ligand 1 (ERRL1)" can be found at page 4, lines 25-26. Support for the definition of "ERR" as "estrogen related receptor (ERR)" can be found at page 1, line 11.

Support for the revised method steps in claim 1 can be found in the disclosure, for example, at page 14, line 20 to page 16, line 4, and in original claim 1.

Claims 1 and 2 have been amended to better reflect the understanding of the invention as an active ingredient in a "therapeutic agent" and/or "pharmaceutical composition" for the treatment of obesity and/or diabetes. Support can be found in the disclosure, for instance, at page 5, lines 17-19 and page 21, line 18 to page 22, line 11, and in original claims 1-2.

Support for the transgenic mouse of amended claim 3 can be found in the disclosure, for example, at page 19, line 21 to page 20, line 3, page 20, line 30 to page 21, line 37, Example 2. 6 at page 31, line 30 to page 33, line 3, and in original claim 3.

No new matter has been added.

II. INFORMATION DISCLOSURE STATEMENT

Attached herewith is an English translation of the Abstract for JP 2002-58489, which is reference AK in the IDS filed February 8, 2005. Kindly consider the reference and return an Examiner-initialed PTO-1449 form indicating such.

As evident from the English Abstract, JP 2002-58489 relates to a method for screening a ligand substance for PGC2-PPARγ complex. In contrast, the present invention relates to a method for screening a substance involving an interaction between EERL1 and ERR. Please note that the PGC2 in JP 2002-58489 is the same as EERL1 of the instant invention. See page 4, lines 7-26 of the instant disclosure. ERRL1 (and PGC2) is nearly the same as PGC-1 beta disclosed in the Spiegelman et al. (WO 00/32215) reference. However, the instant claims are not directed to ERRL1 *per se*. Instead, the instant invention is directed to a method, which is different from that disclosed in JP 2002-58489 and Spiegelman et al. (WO 00/32215).

III. CLAIM OBJECTIONS

On page 3 of the Office Action, claims 1-3 were objected to on the basis that they improperly recite a number of acronyms such as ERRL1, ERR and MCAD without first defining what is meant by these terms.

The present amendment overcomes this objection. As noted above, claims 1-3 have been amended to appropriately recite the definitions for the abbreviated terminology as supported by the disclosure. Thus, the objection is untenable and should be withdrawn.

IV. ENABLEMENT REJECTION

On pages 3-12 of the Office Action, claims 1-3 were rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement.

At the bottom of page 3 of the Action, it was indicated that the Specification is only enabling for a transgenic mouse comprising in its genome a construct comprising nucleic acid encoding ERRL1/PGC-1beta, wherein said mouse is lean and expresses higher levels of ERRL1/PGC-1beta, and a method of using said transgenic mouse for screening candidate substances that fulfill one or more of (a) increase expression of ERRL1; (b) increase transcriptional activity; (c) promote binding of ERR1 to ERR; and (d) increase of MCAD gene

product. The Office further contends the Specification does not enable any other non-human transgenic animal nor any other method for screening for an active ingredient in a drug for obesity and/or diabetes. See the paragraph bridging pages 3-4.

This rejection is respectfully traversed as applied to the amended claims.

First, contrary to the Office's position, the Specification fully describes and enables an *in vitro* screening method using cells. See, for example, the disclosure at page 14, line 20 to page 16, line 4, which describes the *in vitro* method of the amended claims, which calls for using cells to screen for a substance that increases transcriptional activity of nuclear ERR and/or promotes binding of ERRL1 to ERR. The Specification also provides *in vitro* working examples demonstrating the interaction of ERRL and ERR in a cell. See for example, Example 2.4 on pages 29-30. The results of the experiments disclosed therein demonstrate that ERRL1 can function as a protein ligand for ERRs and activate ERR-mediated transcription in cultured cells.

Further, kindly note the procedures and techniques disclosed therein are routine and known in the biotechnological arts. It is respectfully submitted the skilled artisan, upon reading the disclosure and in view of the knowledge in the art, could practice the claimed *in vitro* screening method using such routine techniques without undue experimentation. Thus, contrary to the Office's position, the Specification is enabled for an *in vitro* screening method using cultured cells.

Second, with regard to the *in vivo* aspect of the invention, it is respectfully submitted that the transgenic animal is not essential to the claimed screening method. The animal used in the *in vivo* screening method of the present invention should be the non-transgenic (i.e., wild type) animal. The transgenic animal may be used as a **control** in the *in vivo* screening method. See for instance, page 21, lines 4-7 of the disclosure. At this location, the Specification teaches that such a transgenic animal is not only useful as a control in the claimed screening method, but also a model animal in the elucidation of an anti-obesity or anti-diabetic mechanism at the whole body level. The Specification provides working examples demonstrating such. Thus, contrary to the

Office's position, the Specification is enabling for a screening method using non-transgenic (i.e., wild type) animals.

Third, it is respectfully submitted that the amended claims correspond to the subject indicated as enabled by the Examiner at the bottom of page 3 of the Acton. In particular, the new steps and elements (a) and (b) of amended claim 1 correspond to the subject matter indicated as enabled by the Examiner. In this regard, the method of amended claim 1 calls for treating cells or an animal with a candidate substance and specifying the candidate substance having one or more of the following properties as the target active ingredient substance: (a) promoting the binding of an estrogen related receptor ligand 1 (ERRL1) to estrogen related receptor (ERR); and (b) increasing the transcriptional activity of ERR, as same as the action of ERRL1 for ERR.

Lastly, the transgenic animal of claim 3 has been amended to a transgenic mouse comprising a purified polynucleotide encoding a ligand factor ERRL1 for a nuclear receptor ERR in its genomic DNA and overexpressing the ligand factor ERRL1, wherein said transgenic mouse is lean and hyperphagic. Support can be found in the disclosure, for example, at page 20, line 30 to page 21, line 37, and in original claim 3. Thus, the transgenic animals of the claims are no longer directed to just any non-human animal. Instead, they are directed to the transgenic animal supported by the disclosure.

Therefore, the enablement rejection of claims 1-3 under 35 U.S.C. § 112, first paragraph, is untenable and should be withdrawn.

V. INDEFINITENESS REJECTION

On pages 12-13 of the Office Action, claims 1-2 were rejected under 35 U.S.C. § 112, second paragraph, as indefinite for the recitation of "drug" in claim 1. The Office defines "drug" as "a therapeutic agent; any substance, other than food, used in the prevention, diagnosis, alleviation, treatment, or cure of disease." The Office further contends that the instant invention

appears to contain ingredients other than the active ingredient, which is contrary to the definition of drug.

Applicants respectfully traverse this rejection as applied to the amended claims.

Kindly note the original claims are directed to methods for screening the active ingredient in a drug. It is respectfully submitted the term "drug" is well understood and recognized in the art. See for instance, the disclosure, at page 5, lines 17-19 and page 21, line 18 to page 22, line 11, which describes a formulation of the drug as comprising (for example) the active ingredient and a pharmaceutically acceptable carrier. Thus, the term drug, as disclosed in the Specification and understood in the art, is synonymous to "therapeutic agent" and/or "pharmaceutical composition." Accordingly, it should not matter what other ingredients can be found in the composition referred to as a "drug."

Nonetheless, for the sole purpose of expediting prosecution and not to acquiesce to the rejection, the claims have been amended to better reflect this understanding of the invention as an active ingredient in a "therapeutic agent" and/or "pharmaceutical composition" for the treatment of obesity and/or diabetes.

From this disclosure, the skilled artisan can readily use the standard techniques disclosed in the Specification to screen for a substance which serves as the active ingredient in an agent for the treatment of obesity and/or diabetes, by treating cells or an animal with a candidate substance and specifying the candidate substance having one or more of the following: (a) promoting the binding of an estrogen related receptor ligand 1 (ERRL1) to estrogen related receptor (ERR); and (b) increasing the transcriptional activity of ERR, as same as the action of ERRL1 for ERR. Moreover, it is respectfully submitted that the skilled artisan could do so and thereby practice the invention without undue experimentation.

Thus, the indefiniteness rejection of claims 1 and 2 under 35 U.S.C. § 112, second paragraph, is untenable and should be withdrawn.

VI. ANTICIPATION REJECTIONS

On pages 13-15 of the Office Action, claims 1-3 were rejected under 35 U.S.C. § 102(e) as anticipated by Spiegelman et al. (US Patent application publication 2003/0124598) (published July 3, 2003, effective filing date of November 9, 2001).

On pages 16-17, claims 1-3 were rejected under 35 U.S.C. § 102(b) as anticipated by Spiegelman et al. (WO 00/32215).

These rejections are respectfully traversed as applied to the amended claims.

To anticipate a claim, a cited prior art reference must teach each and every element of the claimed invention. See M.P.E.P. § 2131.01.

Amended claim 1 is directed to a method of screening for a substance which serves as the active ingredient in an agent for the treatment of obesity and/or diabetes, which method comprises: treating cells or an animal with a candidate substance and specifying the candidate substance having one or more of the following properties as the target active ingredient substance: (a) promoting the binding of an estrogen related receptor ligand 1 (ERRL1) to estrogen related receptor (ERR); and (b) increasing the transcriptional activity of ERR, as same as the action of ERRL1 for ERR. Amended claim 2 (depends on claim 1) is directed to a pharmaceutical composition comprising as the active ingredient one or more substances specified by the method of claim 1.

The Spiegelman et al. references disclose a method for screening a substance affecting ERRL1/PGC-1beta. However, the amended claims relate to interaction between ERRL1 and ERR. In fact, the method of amended claim 1 relies on this interaction between ERRL1 and ERR. These properties are relied upon in the method of the present invention for determining the substance to be used as the active ingredient. See elements (a) and (b) of amended claim 1. Moreover, elements (a) and (b) of amended claim 1 are not taught nor suggested in the Spiegelman references. Accordingly, since the Spiegelman references fail to disclose these

properties, including the to interaction between ERRL1 and ERR, the Spiegelman references fail to disclose or suggest the method of the present invention.

Furthermore, amended claim 3 is directed to a transgenic mouse comprising a purified polynucleotide encoding a ligand factor ERRL1 for a nuclear receptor ERR in its genomic DNA and overexpressing the ligand factor ERRL1, wherein said transgenic mouse is lean and hyperphagic. Accordingly, the transgenic mouse of the present invention is defined as "lean and hyperphagic." The Spiegelman references do not teach or suggest a transgenic mouse which is both lean and hyperphagic.

Thus, for the reasons set forth above, the Spiegelman references fail to disclose or suggest each and every element of the claimed invention. For this reason, they cannot anticipate the present invention.

Therefore, the anticipation rejection of claims 1-3 under 35 U.S.C. § 102(e) over Spiegelman et al. (US Patent application publication 2003/0124598) and the anticipation rejection of claims 1-3 under 35 U.S.C. § 102(b) over Spiegelman et al. (WO 00/32215) are untenable and should be withdraw.

CONCLUSION

In view of the foregoing amendments and remarks, it is respectfully submitted that the present application is in condition for allowance and early notice to that effect is hereby requested.

If the Examiner has any comments or proposals for expediting prosecution, please contact the undersigned attorney at the telephone number below.

Respectfully submitted,

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ATTACHMENTS

1. English translation of the Abstract of JP 2002-58489 for reference AK in the IDS filed February 8, 2005.

English translation of Abstract of JP 2002-58489 (reference AK in IDS of 2/8/05).

[Abstract]

[Problem] The problem in this invention is to clarify an anti-diabetes mechanism of TZD, and establish a system for screening a new drug for diabetes.

[Solution] The present invention relates to a method for screening a ligand of PGC2-PPARγ complex, which comprises adding a test substance into a system comprising 1) a fusion protein comprising DNA-binding domain and PGC2, 2) PPARγ and 3) a vector comprising a region recognized by the DNA-binding domain, a promoter and a reporter gene ligated to the promoter, and detecting a transcriptional activity for the PGC2-PPARγ complex. The present invention also relates to the fusion protein used in the screening method and a gene encoding the fusion protein.